

REMARKS / ARGUMENTS

Claims 42, 78, 83, 85 and 87 are amended.

Support for Amendments

Support for amendments may be found throughout the application including the specification as filed. Exemplary support for each amendment is provided for the convenience of the examiner.

Claims 42 and 83 are amended to newly recite, “whereby the bryophyte cell is capable of forming N-linked glycans with terminal 1,4 galactosyl residues.” Support may be found at paragraph [0013], which provides in part,

“Integration of the human beta 1,4-galactosyltransferase into the genome of a double knockout *Physcomitrella patens* plant resulted in a mammalian-like N-linked glycosylation pattern without the plant specific fucosyl and xylosyl residues and with mammalian-like terminal 1,4 galactosyl residues.”

Claims 78 and 87 are amended to recite that the bryophyte plant or bryophyte tissue is from *Physcomitrella patens*. Support may be found as provided above in paragraph [0013]. Further support may be found in paragraph [0014], which provides in part,

“It is a further object to provide an efficient process for the production of heterologous animal proteins comprising animal glycosylation patterns, particularly human proteins comprising human glycosylation patterns in bryophytes, such as *Physcomitrella patens*.”

Claim 85 is amended to depend from a pending claim, specifically claim 83.

Introduction of the Invention

The present invention is directed towards a transformed bryophyte cell from *Physcomitrella patens* that is incapable of forming N-linked glycans with 1,3-linked fucosyl and

1,2-linked xylosyl residues. Thus the claims are directed towards a double knockout of the endogenous alpha 1,3-fucosyl transferase and beta 1,2-xylosyl transferase sequences in *Physcomitrella patens*. As such, endogenous glycosylation patterns associated with bryophytes are lacking. In further embodiments the bryophyte cell is capable of forming N-linked glycans with terminal 1,4 galactosyl residues, which mimics a human-like glycosylation pattern. This is accomplished through the expression of a human beta 1,4 galactosyltransferase within the transformed bryophyte cell. In still further embodiments, a bryophyte plant or tissue from *Physcomitrella patens* is provided, which includes the transformed bryophyte cell.

Examiner Interview Summary

Applicants thank the examiner for the interview conducted on January 13, 2010 with Applicants' attorney of record, Raymond Wagenknecht (Reg. no. 50948). In the interview each of the rejections were discussed as well as differences between bryophyte and human glycosylation patterns and proposed changes to the title and claims as suggested by Raymond Wagenknecht. No exhibits or materials were provided.

Although no final decision was reached regarding the patentability of the claims an amendment correlating the function of a human beta 1,4 galactosyltransferase with the bryophyte's ability to form N-linked 1,4 galactosyl residues was considered likely to traverse the enablement and written description rejections of claims 42 and 83. Raymond Wagenknecht also proposed an alternative title that would be directed towards independent claim 38, which provides a double knockout of alpha 1,3-fucosyl and 1,2-xylosyl transferases in a bryophyte cell but does not require the expression of an enzyme involved in glycosylation.

Response to Specification Objections

The examiner objects to the title as not being sufficiently descriptive. The examiner suggests the following title, "Transformed bryophyte cell expressing enzymes involved in glycosylation for the production of heterologous proteins."

Although the suggested title is descriptive of dependent claims, independent claim 38

does not require expression of enzymes involved in glycosylation but instead is directed towards a transformed bryophyte cell having a disrupted endogenous alpha 1,3-fucosyl and beta 1,2-xylosyl transferase encoding sequence. These disruptions result in the inability of the bryophyte to form 1,3 fucosyl and 1,2 xylosyl residues. Accordingly, the title is amended to recite,

“Transformed bryophyte cell having disrupted endogenous alpha 1,3-fucosyl and beta 1,2-xylosyl transferase encoding nucleotide sequences for the production of heterologous glycosylated proteins”

Applicants respectfully request the objection be withdrawn.

Response to New Claim Objections

The examiner objects to claims 40, 42, 78, 83, 84 and 87 as being substantial duplicates. For completeness, claims 40 and 84 are canceled.

Claims 42 and 78 depend from claim 38 and claims 83 and 87 depend from claim 39. Claim 38 differs from claim 39 in that claim 39 requires the bryophyte cell include a nucleic acid sequence, which encodes a glycosylated polypeptide, operably linked to an exogenous promoter that drives expression in the bryophyte cell; whereas claim 38 does not. Claim 38 requires the bryophyte cell being incapable of forming N-linked glycans with 1,3-linked fucosyl and 1,2-linked xylosyl residues. Thus, whereas claim 38 refers to the inability to form N-linked 1,3-fucosyl and 1,2 xylosyl residues, claim 39 additionally requires a nucleotide sequence linked to an exogenous promoter that encodes a glycosylated polypeptide.

Accordingly, claims 42, 78, 83 and 87 are not substantial duplicates. As such, Applicants respectfully request the objections be withdrawn and the claims allowed.

Claims 48 and 50 are rejected as being dependent on a rejected base claim, namely claim 39. Since the rejection of claim 39 is traversed as provide below, Applicants respectfully request the allowance of claims 48 and 50.

Response to Double Patenting Rejection

Claims 38-40, 42, 78, 81, 83, 84 and 89 are provisionally rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 1-7, 16, 23, 24, 28 and 29 over copending US application serial no. 11/995,191.

To expedite allowance, Applicants provide a terminal disclaimer over US application serial no. 11/995,191. Accordingly, Applicants respectfully request the rejection be withdrawn and the claims allowed.

Response to Rejections Under 35 U.S.C. § 112, 2nd Paragraph

The definiteness of language employed must be analyzed not in a vacuum, but in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing ordinary skill in the art. Allen Archery Inc. v. Browning Mfg. Co., 2 USPQ2d 1490, 1494 (Fed. Cir. 1987). “If the claims, read in light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the courts can demand no more.” North Am. Vaccine, Inc. v. American Cyanamid Co., 28 USPQ2d 1333, 1339 (Fed. Cir. 1993).

Claims 40 and 84, and thus 85-86 stand rejected under 35 U.S.C. § 112, 2nd paragraph for being indefinite. Specifically, the examiner objects to the phrase “human glycosylation pattern.”

One skilled in the art would understand that a human glycosylation pattern is the arrangement of residues consistent with expression of endogenous human proteins. However, to expedite allowance of the application claims 40 and 84 have been canceled and claim 85, from which claim 86 depends, is amended to depend from pending claim 83. Accordingly, Applicants respectfully request the rejections be withdrawn and claims 85-86 allowed.

Claims 78 and 87 are rejected under 35 U.S.C. § 112, 2nd paragraph for being indefinite because claims 78 and 87, which recite a bryophyte plant or bryophyte tissue depend from claim 38, which recites the particular transformed bryophyte cell *Physcomitrella patens*.

Claims 78 and 87 are amended to refer to the bryophyte *Physcomitrella patens*.
Accordingly, Applicants respectfully request the rejection be withdrawn and the claims allowed.

Claim 96 is rejected under 35 U.S.C. § 112, 2nd paragraph for being indefinite due to the recitation of GenBank Accession numbers. Though GenBank Accession numbers are accepted as an international standard format for providing sequence information and provide suitable information to which one skilled in the art could readily identify the claimed sequence, Applicants cancel claim 96 to expedite allowance.

Response to Claim Rejections Under 35 U.S.C. § 112, 1st Paragraph

Enablement Rejections

The examiner rejects claims 40, 42, 78 and 83-87 under 35 U.S.C. § 112, first paragraph, as not being enabled. Specifically, the examiner argues the application does not provide enablement for a transformed bryophyte from *Physcomitrella patens* including any functional human beta 1,4-galactosyltransferase including variants, mutants and recombinants capable of producing any human glycosylation pattern with respect to claims 40, 42, 83 and 84 and any bryophyte plant or tissue including a cell from *Physcomitrella patens* with respect to claims 78 and 87. On pages 11 and 12 of the Office Action the examiner argues there are various forms of glycosylation including N-glycosylation, O-glycosylation as well as carbohydrates that are components of glycosphosphatidylinositol anchor for securing proteins to cell membranes and there are varying GalT transferases having distinct biological functions.

The enablement requirement is met when the specification teaches one of ordinary skill in the art how to make and use the invention. The general policy of the enablement requirement is to ensure the claimed invention is communicated in such a way that the public may understand and perhaps build on it. However, a detailed report regarding how to make and use the invention is unnecessary if a person of ordinary skill in the art could understand the invention without such an explanation. For instance the CCPA has stated that “not every last detail is to be described,

else patent specifications would turn into production specifications, which they were never intended to be.” In re Gay, 309 F.2d 769 (C.C.P.A. 1962). This is consistent with the discussion provided in Ajinomoto Co., Inc. v. Archer-Daniels-Midland Co., 228 F.3d 1338 (Fed. Cir.), *cert denied*, 532 U.S. 1019 (2001), which stated,

“Requiring inclusion in the patent of known scientific/technological information would add an imprecise and open-ended criterion to the content of patent specifications, could greatly enlarge the content of patent specifications and unnecessarily increase the cost of preparing and prosecuting patent applications, and could tend to obfuscate rather than highlight the contribution to which the patent is directed. A patent is not a scientific treatise, but a document that presumes a readership skilled in the field of the invention.”

Further, to be enabling, the specification must teach those skilled in the art how to make and use the invention without undue experimentation. Genentech, Inc. v. Novo Nordisk, A/S, 108 F.3d 1361, 1365, 42 USPTO2d 1001, 1004 (Fed. Cir.), *cert. denied*, 522 U.S. 963 (1997). Factors considered whether undue experimentation is required include 1) the quantity of experimentation necessary, 2) the amount of direction or guidance provided, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative level of skill of those in the art, 7) the predictability of the art, and 8) the breadth of the claims. In re Wands, 858 F.2d 731 (Fed. Cir 1988).

Claim 40 is canceled and Claims 42 and 83, from which claims 78, and 85-87 depend, are amended to include that the bryophyte cell, which includes a nucleotide sequence encoding a functional human beta 1,4 galactosyltransferase, is capable of forming N-linked glycans with terminal 1,4 galactosyl residues. With respect to Wands factors 2 and 3, the specification provides substantial direction and guidance how to accomplish the recitation. Specifically, the examples section teaches the generation and testing of suitable transgenic plants having the desired dysfunctional endogenous alpha 1,3-fucosyl transferase and beta 1,2-xylosyl transferase together with a functional human beta 1,4 galactosyltransferase that results in terminal 1,4 galactosyl residues. For instance pages 42 and 43 confirm the activity of human beta 1,4 galactosyltransferase in *Physcomitrella patens* through analysis of N-glycan patterns of proteins in double knock out transgenic plants using MALDI-TOF mass spectrometry,

“The N-glycans of *Physcomitrella patens* WT exhibit the typical structural features of plant N-glycans... Three transgenic plants were analyzed... The peak at 2235 found in WT describing the (GF)(GF)XF structure was shifted to mass peak of 1665 in the N-glycan pattern of the transgenic plants confirming the activity of human beta 1,4 galactosyltransferase in *Physcomitrella patens* as well as the loss of 1,3 linked fucosyl and 1,2 linked xylosyl residues.”

Since amount of direction in the examples section is quite high, the amount of experimentation needed by one skilled in the present art, Wands factor 1, would be correspondingly reduced. Further with respect to Wands factors 4-7, although nature of the invention is biological and can thus be considered complex, the state of the art and the relative level of skill of those in the present art is quite high. For instance, commercial kits and apparatuses to obtain and sequence DNA are commonly available and techniques that may be used to test for N-linked terminal 1,4 galactosyl residues are also known. That is, laboratories regularly perform PCR, MALDI-TOF mass spec, and various cloning techniques, which demonstrates a high level of skill.

With respect to Wands factor 8, the breadth of the claims, Applicants have amended the claims to include structure features resulting from a functional human beta 1,4 galactosyltransferase. That is, Applicants have specifically included the requirement that the bryophyte is capable of forming N-linked glycans with terminal 1,4 galactosyl residues. As such, the structural features corresponding to a functional human beta 1,4 galactosyltransferase are specifically set forth and can be identified by the skilled artisan.

Since the specification teaches the generation and testing of the claims as amended, the claims are clearly enabled. Accordingly, Applicants respectfully request the rejections be withdrawn and the claims allowed.

Written Description Rejections

The examiner rejects claims 40, 42, 78 and 83-87 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Specifically, the examiner argues the claims encompass an extremely large number of polynucleotides and encoding polypeptides of undefined structure, the polypeptides having a functional human beta 1,4-galactosyltransferase

including variants, mutants and recombinants capable of producing any human glycosylation pattern and furthermore any bryophyte plant or bryophyte tissue comprising the transformed *Physcomitrella patens*. For completeness, claims 40 and 84 are canceled

The written description requirement places in possession of the public what the applicant considers to be the invention for which a patent is being sought. As stated by the examiner (Quoting Univ. of Calif. V. Eli Lilly), "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." The examiner also refers to MPEP § 2163, in that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus.

Claims 42 and 83, from which claims 78 and 85-87 depend, are amended to recite, "whereby the bryophyte cell is capable of forming N-linked glycans with terminal 1,4 galactosyl residues." Accordingly, while the examiner argues the written description requirement is not satisfied prior to amendment, as set forth in the claims a bryophyte including a human beta 1,4 galactosyltransferase capable of forming N-linked glycans with terminal 1,4 galactosyl residues provides specific structural features together with the enzyme's function, which fulfills the written description requirement.

Claims 78 and 87 are amended to recite a bryophyte plant or tissue from *Physcomitrella patens*. Thus, claims 78 and 87 as amended are directed to the particular bryophyte *Physcomitrella patens* and not any bryophyte as examined.

For completeness, claim 85 is also amended to depend from pending claim 83.

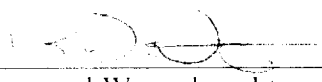
Accordingly, Applicants submit the claims as amended clearly meet the written description requirement. Thus, Applicants respectfully request the rejections be withdrawn and the claims allowed.

Conclusion

In view of the amendments and arguments set forth above, Applicants respectfully request the withdrawal of each rejection and the request a Notice of Allowance be issued for the instant application. Question regarding the invention may be directed to the attorney of record.

Respectfully submitted,

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Date


Raymond Wagenknecht
Reg. no. 50948

Biotech Beach Law Group PC
5677 Oberlin Dr., Ste 204
San Diego, CA 92121
(858) 587-2510